Remarks

Claims 25-37, 40-44, 47-51, 54-58, and 61-74 are pending in the instant application.

Applicants have amended claims 37, 40, 44, 47, 51, 54, 58, and 61 to replace the phrase "capable of generating or selecting an antibody" with the phrase "activates the gamma activating sequence promoter element." Applicants have canceled claims 38-39, 45-46, 52-53, and 59-60 without prejudice or disclaimer. Applicants reserve the right to pursue the canceled subject matter in one or more continuing applications. No new matter has been added.

I. Finality of the Office Action

Applicants respectfully assert that the finality of the Office Action (Paper No. 9) was premature. Applicants note that the Examiner has both cited new references and expanded her arguments in the current Office Action with respect to the 35 U.S.C. § 112, first paragraph rejections. Citing new references and/or expanding arguments in a second Office action can prevent that Office action from being made final. *See* M.P.E.P. § 2164.04. In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the finality of the rejection.

II. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

A. Enablement

The Examiner has maintained the rejection of claims 25-74 under 35 U.S.C. § 112, first paragraph. *See* Paper No. 9, page 3, section 6.1. In particular, the Examiner alleges:

> While there is no reason to doubt the assertion that the gene encoding the polypeptide could be used as a cancer marker and is therefore credible, this is not sufficient to enable the use of the polypeptide. The specification states that the gene is expressed primarily in ovarian tissue, and to a lesser extent in breast and prostate tissue. However, absent information on how many tissue samples were analyzed, and the degree of expression in cancer tissue relative to normal tissue, one of ordinary skill in the art would not conclude that this gene or encoded polypeptide would be useful as cancer markers.

Paper No. 9, page 5, lines 3-10.

Applicants respectfully disagree and traverse.

Applicants point out that the Examiner is not questioning that the specification teaches how to make the claimed invention, only whether the "how to use" portion of the

enablement requirement has been met. The standard for enablement is whether the experimentation needed to practice the invention is undue or unreasonable. *See* M.P.E.P. § 2164.01. Applicants reiterate that, at the time the application was filed, one of ordinary skill in the art would have readily been able to make and use the invention as a cancer diagnostic without undue experimentation by following the teachings of the specification. Indeed, all that would be needed to practice the invention would be, for example, to perform Western blotting or quantitative RT-PCR to determine whether expression of the claimed protein was increased in particular cancerous tissue samples relative to normal, non-diseased samples. Whether the skilled artisan would be convinced that the invention, if practiced as taught in the specification, would be useful as a cancer diagnostic may be an issue of utility, but it is clear that the specification fully enables that use of the claimed invention. Moreover, the Examiner has noted that "there is no reason to doubt the assertion that the gene encoding the polypeptide could be used as a cancer marker" (Paper No. 9, page 5, lines 4-5), agreeing with Applicants that the utility requirement of 35 U.S.C. § 101 has been fully met.

To make a proper enablement rejection, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. M.P.E.P. § 2164.04; *see also, In re Wright*, 999 F.2d 1557, 1561-1562, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). In the instant rejection, the Examiner asserts the specification, while asserting a proper utility as a marker for cancer, does not sufficiently enable one of ordinary skill in the art how to use the gene or the polypeptide encoded by the gene as a cancer diagnostic. Specifically, the Examiner appears to require that Applicants present statistical evidence demonstrating the efficacy of the claimed protein as a cancer diagnostic. In support of this position, the Examiner cited two references wherein the usefulness and relevance of cancer markers in a patient population was demonstrated by statistical evidence.

In response, Applicants note that statistical evidence is neither the legal requirement nor the standard for patentability. As stated earlier, the test for enablement is whether one of ordinary skill in the art can practice the claimed invention without undue or unreasonable experimentation. Demonstrating statistical certainty or providing statistical evidence/analysis is not a requirement for the patentability of one's invention.

The Examiner alleges that based on the teachings of Ferrari *et al.* and Clark *et al.*, one of ordinary skill would recognize that "a minimal number of samples must be analyzed before concluding that a particular gene would be useful as a cancer marker." *See* Paper No. 9, page 6, lines 18-19. Applicants disagree. Among other things, Ferrari *et al.* teach, "the

clinical value of these molecular indicators of metastasis remains to be established over time," while Clark *et al.* teach that PIP is a potential marker of human breast cancer micrometastasis. The statistical evidence presented by the authors is used to support their conclusions, not establish them. Indeed, PIP, PSA and PSM were previously determined to be putative markers for tumors prior to the publication of Ferrari *et al.* and Clark *et al.* Furthermore, the Examiner alleges, "[c]ontrary to the Applicant's argument, the determination of a cancer marker must be based on studying results from a considerable number of patients and statistical analysis." *See* Paper No. 9, page 6, lines 19-21. As Applicants have noted above, neither the Ferrari *et al.* nor Clark *et al.* corroborate this statement, and the Examiner has not identified additional support for this position.

Thus, Applicants maintain that the Examiner has failed to provide sufficient evidence pointing out the lack of enablement of the instant specification. A patent Applicant's specification disclosure that contains a teaching of how to make and use the invention must be taken as enabling unless the Patent Office provides sufficient reason to doubt the accuracy of the disclosure. *See In re Marzocchi*, 439 F.2d. 220, 223-224, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971). Accordingly, Applicants assert that the claims fully meet the enablement requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection of claims 25-74 be reconsidered and withdrawn.

B. Written Description

Claims 37-64 are rejected under 35 U.S.C. § 112, first paragraph. *See* Paper No. 9, page 7, section 6.2. In particular, it was asserted:

> [Claims 37-64 contain] subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Paper No. 9, page 7, lines 12-15.

Applicants respectfully disagree and traverse.

Applicants maintain that the previous pending claims fully comply with 35 U.S.C. § 112, first paragraph. Nevertheless, Applicants have amended claims 37, 40, 44, 47, 51, 54, 58, and 61, such that the claimed protein variants must activate the gamma activating sequence promoter element. Support for this phrase may be found at page 65, lines 17-19 of the specification as filed. Since Applicants have disclosed a single species representative of

the entire genus, one of ordinary skill in the art would reasonably conclude that Applicants were in possession of the claimed genus. Accordingly, Applicants believe the Examiner's rejection has been overcome.

Applicants submit that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the Examiner's rejection of claims 37-64 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Conclusion

Applicants respectfully request the amendments and remarks of the present response be entered and made of record in the present application. In view of the foregoing amendment and remarks, Applicants believe they have fully addressed the Examiner's concerns and that this application is now in condition for allowance. An early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicants would expedite the allowance of this application.

Applicants believe that there are no fees due in connection with the filing of this paper. However, should a fee be due, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the appropriate fee should also be charged to our Deposit Account.

Respectfully submitted,

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